

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) Method for identifying 5-methylcytosine positions in a sample genomic DNA, said method ~~comprising~~ consisting of the steps of:

a) chemically treating a sample genomic DNA obtained from at least one cell, cell line, tissue or individual in such a way that cytosine and 5-methylcytosine react differently and form products with different base pairing behavior,

b) amplifying, by means of a polymerase reaction, a segment of the sample genomic DNA obtained in step a),

c) performing steps a) and b) on a reference genomic DNA,

d) forming heteroduplexes from the amplified segments produced in steps b) and c),

e) introducing a detectable label into the heteroduplexes of step d) by means of a reaction, which is specific for non-complementary base pairs, and

f) determining the position of 5-methylcytosine in the sample genomic DNA based on the presence and position of the detectable label.

2. (Previously presented) Method according to claim 1, further characterized in that only positions at which cytosine methylation is variable between different cells, cell lines, tissues or individuals are used for the identification of differences in cytosine methylation patterns between different cells, cell lines, tissues and individuals.

3. (Previously presented) Method according to claim 1, further characterized in that disulfite (bisulfite, pyrosulfite) is utilized in the chemical treatment of a sample genomic DNA in step a).

4. (Previously presented) Method according to claim 1, further characterized in that genomic DNA of several individuals, tissues, cell lines or cells is amplified jointly in step b) of claim 1.

5. (Previously presented) Method according to claim 1, further characterized in that the genomic DNA of a plurality of samples are treated and amplified according to steps a) and b).

6. (Previously presented) Method according to claim 1, further characterized in that by formation of heteroduplexes from the DNA of different individuals, tissues, cell lines or cells, erroneous base pairings are produced at the positions at which a 5-methylcytosine was located in the sample genomic DNA.

7. (Previously presented) Method according to claim 1, wherein the reference genomic DNA is methylated at every CpG position.

8. (Previously presented) Method according to claim 1, further characterized in that at least one of the genomic DNAs is an unmethylated reference DNA and where in step d), the erroneous base pairings within the heteroduplex occur at those positions at which 5-methylcytosine was located in the other genomic DNA.

9. (Previously presented) Method according to claim 30, further characterized in that in step e) the nucleic acid backbone of the heteroduplex is specifically cleaved at the non-complementarily base paired positions by enzymatic means.

Claim 10 (Canceled).

11. (Previously presented) Method according to claim 30, further comprising in e) measurement of the size(s) of the nucleic acids and wherein the location and/or presence of cleaved positions is therefrom inferred, thereby enabling the identification of the position(s) of methylcytosines differentially methylated between the genomic DNAs.

12. (Previously presented) Method according to claim 11, further characterized in that analysis of size (molecular weight) of the DNA fragments is conducted by means of mass spectrometry.

13. (Previously presented) Method according to claim 12, further characterized in that the fragments are analyzed by means of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF).

14. (Original) Method according to claim 12, further characterized in that the fragments are analyzed by means of electrospray ionization mass spectrometry (ESI).

15. (Previously presented) Method according to claim 13, further characterized in that the size of the nucleic acids produced in step e) is adapted to the performance capacity of the mass spectrometer.

16. (Previously presented) Method according to claim 15, further characterized in that in step b) a plurality of PCRs of a gene segment are carried out and wherein PCR primers of each PCR are positioned such that they are set stepwise to other PCR primers used in the plurality of PCRs thereby producing a series of amplificate nucleic acids of different sizes at least one of which is within the mass range detectable by means of mass spectrometry.

Claim 17 (Canceled).

18. (Previously presented) Method according to claim 1, further characterized in that in step b) one primer of the polymerase reaction is provided with a chemical function that enables the polymerase reaction product to be immobilized on a surface.

19. (Previously presented) Method according to claim 1, further characterized in that the product of step b) is transferred to different reaction vessels and the surfaces of the reaction vessels are chemically treated such that the product can be bound thereon.

20. (Previously presented) Method according to claim 1, further characterized in that products of different individuals that are produced in step c) are transferred into different reaction vessels the surfaces of which are chemically treated such that said products can be bound thereon.

21. (Previously presented) Method according to claim 1, further characterized in that an enzyme which forms a complex with a non-complementary base pair is used for step e).

22. (Original) Method according to claim 21, further characterized in that this enzyme is MutS.

23. (Original) Method according to claim 21, further characterized in that the enzyme bears a label, by which a complex can be displayed.

24. (Original) Method according to claim 21, further characterized in that the label is a fluorescence label, a chemiluminescence label, a mass label or a photochemically cleavable mass label.

Claim 25 (Canceled).

26. (Currently amended) A method for identification of 5-methylcytosine positions in genomic DNA, ~~characterized by the fact that~~ consisting of the following steps ~~are conducted~~:

a) the genomic DNA of a cell, a cell line, a tissue or an individual is chemically treated in such a way that cytosine and 5-methylcytosine react differently and form products with different base pairing behaviors,

b) a nucleic-acid segment is amplified by a polymerase reaction wherein the amplificate is fluorescently labeled and provided with a chemical function thereby enabling the immobilization of the amplificate on a surface,

c) the genomic DNA of at least one other cell, cell line, tissue or individual or any reference DNA is treated according to steps a) and amplified by a polymerase reaction such that the same genomic locus as in b) is amplified,

d) heteroduplexes are formed from at-least two amplified products of steps b) and c) wherein erroneous base pairings occur at the positions at which differentially methylated cytosines were located in the genomic DNAs,

e) a chemical mismatch cleavage reaction is carried out wherein the fluorescent label of cleaved nucleic acids is removed by washing,

f) the cleaved nucleic acids are analyzed by mass spectrometry,

g) the presence or presence and position of 5-methylcytosine within the genomic DNA of a) or b) is deduced from the length of the cleaved nucleic acids.

27. (Currently amended) A method for identification of 5-methylcytosine positions in genomic DNA, ~~characterized by the fact that~~ consisting of the following steps ~~are conducted~~:

a) the genomic DNA of a cell, a cell line, a tissue or an individual is chemically treated in such a way that cytosine and 5-methylcytosine react differently and form products with different base pairing behaviors,

b) a nucleic-acid segment is amplified by a polymerase reaction wherein the amplificate is fluorescently labeled and provided with a chemical function thereby enabling the immobilization of the amplificate on a surface,

c) the genomic DNA of at least one other cell, cell line, tissue or individual or any reference DNA is treated according to steps a) and amplified by a polymerase reaction such that the same genomic locus as in b) is amplified,

d) heteroduplexes are formed from at-least two amplified products of steps b) and c) wherein erroneous base pairings occur at the positions at which differentially methylated cytosines were located in the genomic DNAs,

e) a detectable label is introduced into the heteroduplex by an enzymatic reaction, which is specific for non-complementary base pairs,

f) either the labeled or non-labeled nucleic acids are analyzed by mass spectrometry,

g) the presence or presence and position of 5-methylcytosine within the genomic DNA of a) or b) is deduced.

Claims 28-29 (Canceled).

30. (Currently amended) A method for identifying 5-methylcytosine positions in a sample genomic DNA, said method ~~comprising~~ consisting of the steps of:

a) chemically treating a sample genomic DNA obtained from at least one cell, cell line, tissue or individual in such a way that cytosine and 5-methylcytosine react differently and form products with different base pairing behavior,

b) amplifying, by means of a polymerase reaction, a segment of the sample genomic DNA obtained in step a),

c) performing steps a) and b) on a reference genomic DNA,

d) forming heteroduplexes from the amplified segments produced in steps b) and c), wherein erroneous base pairings occur at positions at which differentially methylated cytosines were located in the sample and reference genomic DNAs,

e) cleaving the heteroduplexes of step d) by a chemical mismatch cleavage reaction, and

f) determining the position of 5-methylcytosine in the sample genomic DNA based on the cleavage of heteroduplexes in step e).